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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,102	01/25/2001	Roger Craig	10069/1062	5353
29933	7590	10/06/2003	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			COUNTS, GARY W	
		ART UNIT	PAPER NUMBER	
		1641	14	

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/770,102	CRAIG, ROGER
<b>Examiner</b>	<b>Art Unit</b>	
Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 27 June 2003.

2a)  This action is **FINAL**.                    2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## **Disposition of Claims**

4)  Claim(s) 1-5,7-13,27,28,30,32-34,51 and 52 is/are pending in the application.  
4a) Of the above claim(s) 35-50 and 55-76 is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1-5,7-13,27,28,30,32-34,51 and 52 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_  
4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.  
5)  Notice of Informal Patent Application (PTO-152)  
6)  Other: \_\_\_\_\_

## DETAILED ACTION

### Status of the claims

The amendment filed June 27, 2003 is acknowledged and has been entered.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-13, 27, 28, 30, 32-34, 51 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and 51 is vague and indefinite because it is unclear how dissociation is detected. It appears that in order to detect the dissociation of the binding partner polypeptides, the binding partner polypeptides would have to already be bound to something else and this binding detected. Then the detection of dissociation of the binding partner polypeptides would be performed.

Claim 11 is vague and indefinite because it is unclear what relationship exists between the tagged binding partner, the detection molecule and the binding partner of step (ii) tagged. Are there three labels present in the assay and if so are they the same or different?

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1, 3, 4, 7, 8, 27, 28, 30, 32-34 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al (WO 98/44350) in view of Colyer (WO 99/11774).

Blau et al disclose methods for detecting protein-protein interactions. Blau et al specifically disclose that the term proteins and polypeptides are interchangeable (p. 9). Blau et al disclose that the methods of the invention can be used to study other molecules which influence the interaction between the binding partners (p. 23, lines 11-12). Blau et al disclose the phosphorylation of one of the binding partners endows it to associate with another of the binding partners (p. 23, line 30 – p. 24 line 3). Blau et al disclose that the interactions can be detected by using reporter subunits (tag) which produce a chromogenic, fluorescent or luminescent signals. (p. 19, lines 20-27). Blau et al disclose that the reporter subunits may comprise fluorophores, which are capable of detectable resonance energy transfer when they are closely associated (p. 14, lines 27-32). Blau et al disclose that the methods can be used to study agonists or antagonist of a binding interaction (p. 23).

Blau et al differ from the instant invention in failing to teach a detector molecule comprising a first region that associates with the tagged binding partner polypeptide and a second region comprising one or more reporter molecules. Blau et al also fails to teach detecting binding or dissociation of the binding partner polypeptides and the tagged binding partner polypeptides in both the presence and absence of candidate modulators.

Colyer et al disclose a method for monitoring the activity of an enzyme comprising monitoring the addition or removal of a moiety (p. 15). Colyer et al disclose mixing a labeled (tag) polypeptide comprising a coiled-coil with its binding partner. Colyer et al disclose mixing with the labeled polypeptide a second coiled-coil comprising a label (detection molecule) (see page 39 and 50). Colyer et al disclose that this second coiled-coil comprises a linker, which is associated with the labeled polypeptide. Colyer et al disclose that these polypeptides comprise sites for the addition or removal of a moiety (p 6). Colyer et al disclose incubating the polypeptides with an appropriate modifying enzyme and measuring the change in energy transfer between the polypeptide and its binding partner. Colyer et al also disclose methods for screening a candidate modulator (p. 17-18). Colyer et al also teach detecting binding or dissociation of the binding partner in both the presence and absence of a candidate modulator (p. 18). Colyer et al disclose that the use of these coiled-coil tag and detection molecules provides for efficient means of monitoring and/or modulating post-translational protein modification and provides for techniques whereby the addition/removal of a modifying group can be monitored continuously during real time to provide a dynamic assay system that also has the ability to resolve spatial information (p. 5).

It would have been obvious to one of ordinary skill in the art to incorporate detection molecules, tag molecules and candidate modulators as taught by Colyer et al into the method of Blau et al because Colyer et al shows that the use of these coiled-coil tag and detection molecules provides for efficient means of monitoring and/or modulating post-translational protein modification and provides for techniques whereby

the addition/removal of a modifying group can be monitored continuously during real time to provide a dynamic assay system that also has the ability to resolve spatial information.

3. Claims 2 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al in view of Colyer et al as applied to claims 1, 3, 4, 7, 8, 27, 28, 30, 32-34 and 51 above, and further in view of Heroux et al (US 6,312,896)

See above for teachings of Blau et al and Colyer et al.

Blau et al and Colyer et al differ from the instant invention in failing to teach the binding partner polypeptides immobilized on a solid support.

Heroux et al disclose methods for measuring the activity of enzymes. Heroux et al disclose mixing two substrates and an enzyme which catalyzes a change in the substrate molecule (for example phosphorylation of a protein) that induces the substrate to bind to a second molecule (col 11, lines 1-62). Heroux et al disclose that these substrates can be polypeptides and that these polypeptides can contain natural and unnatural units (col 12, lines 1-32). Heroux et al also disclose that the substrates can be immobilized on a solid support (Fig. 2). Heroux et al disclose that the invention can be used to assay an enzyme inhibitor and/or to measure the inhibitory ability of test compound. Heroux et al discloses that the immobilization of the polypeptide provides for a simple, accurate and reliable assay for measuring enzyme activity in a sample.

It would have been obvious to one of ordinary skill in the art to immobilize polypeptides to a solid support as taught by Heroux et al into the method of Blau et al

because Heroux et al discloses that the immobilization of the polypeptides provides for a simple, accurate and reliable assay for measuring enzyme activity in a sample.

4. Claims 5 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al in view of Colyer et al as applied to claims 1, 3, 4, 7, 8, 27, 28, 30, 32-34 and 51 above, and further in view of Levin et al (US 2002/0197696).

See above for the teachings of Blau et al in view of Colyer et al.

Blau et al and Colyer et al differ from the instant invention in failing to teach monitoring the rate of diffusion of the fluorescent molecule.

Levin et al disclose Fluorescence Correlation Spectroscopy (FCS), which measure the average diffusion rate of a fluorescent molecule within a small sample volume. Levin et al disclose that FCS can be applied to protein-ligand interaction (p. 13, paragraph 0143).

It would have been obvious to one of ordinary skill in the art to incorporate Fluorescence Correlation Spectroscopy as taught by Levin et al into the modified method of Blau et al because Levin et al teaches that FCS provides for the average diffusion rate of a fluorescent molecule within a small sample volume and that it can be applied to protein-ligand interactions.

5. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blau et al in view of Colyer et al as applied to claims 1, 3, 4, 7, 8, 27, 28, 30, 32-34 and 51 above, and further in view of Wild et al (The Immunoassay Handbook, Signal Generation and Detection Systems, p. 63, 1994).

See above for teachings of Blau et al and Colyer et al.

Blau et al and Colyer et al differ from the instant invention in failing to teach radioactive molecules and measuring radioactivity.

Wild et al teach the use of radioactive labels in immunoassays and the measurement of radioactivity. Wild et al teach that radioactive labels are thought of as powerful beacons, detectable at even lower concentrations than are usually measured by immunoassay.

It would have been obvious to one of ordinary skill in the art to incorporate radioactive labels and measurement of radioactivity as taught by Wild et al into the modified method of Blau et al because Wild et al teaches radioactive labels are thought of as powerful beacons, detectable at even lower concentrations than are usually measured by immunoassay.

#### ***Response to Arguments***

6. Applicant's arguments with respect to claims 1-4, 27, 28 and 32-34, concerning Blau et al (WO 98/44350 and Heroux et al (US 6,312,896) have been considered but are moot in view of the new ground(s) of rejection.

#### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts  
Examiner  
Art Unit 1641  
September 23, 2003



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09/26/03